



SEQUENCE LISTING

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TECH CENTER 1000, 2900

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<110> Wang, Elizabeth

<120> REGULATION OF EPITHELIAL TISSUE BY HEDGEHOG-LIKE
POLYPEPTIDES, AND FORMULATIONS AND USES RELATED THERETO

<130> CIBT-P03-031

<140> 09/151,999

<141> 1998-09-11

<150> 08/955,552

<151> 1997-10-20

<160> 28

<170> PatentIn Ver. 2.0

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Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala	
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Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	
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ctc	atg	aca	cag	aga	tgc	aaa	gac	aag	ctg	aac	tcg	ctg	gcc	atc	tct	336
Leu	Met	Thr	Gln	Arg	Cys	Lys	Asp	Lys	Leu	Asn	Ser	Leu	Ala	Ile	Ser	
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Val	Met	Asn	His	Trp	Pro	Gly	Val	Lys	Leu	Arg	Val	Thr	Glu	Gly	Trp	
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Asp	Glu	Asp	Gly	His	His	Phe	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	
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Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Lys	Ser	Lys	Tyr	Gly	Thr	
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Leu	Ser	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu	
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Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala	
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gcg	aaa	tct	ggg	ggc	tgt	ttc	cca	ggt	tcg	gct	ctg	gtc	tcg	ctc	cag	624
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Asp	Gly	Gly	Gln	Lys	Ala	Val	Lys	Asp	Leu	Asn	Pro	Gly	Asp	Lys	Val	
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Leu	Ala	Ala	Asp	Ser	Ala	Gly	Asn	Leu	Val	Phe	Ser	Asp	Phe	Ile	Met	
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Phe	Thr	Asp	Arg	Asp	Ser	Thr	Thr	Arg	Arg	Val	Phe	Tyr	Val	Ile	Glu	
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Thr	Gln	Glu	Pro	Val	Glu	Lys	Ile	Thr	Leu	Thr	Ala	Ala	His	Leu	Leu	
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Phe	Val	Leu	Asp	Asn	Ser	Thr	Glu	Asp	Leu	His	Thr	Met	Thr	Ala	Ala	
		275					280					285				
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Tyr	Ala	Ser	Ser	Val	Arg	Ala	Gly	Gln	Lys	Val	Met	Val	Val	Asp	Asp	

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Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu			
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Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser			
	355	360	365
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Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn			
	370	375	380
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Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr			
385	390	395	400
tgg ctt ttg gac agc aac atg ctt cat cct ttg ggg atg tca gta aac			1248
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ctg gta tgc tcg gga ctg gcg tgc gga ccg ggc agg ggg ttc ggg aag			96
Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys			
	20	25	30
agg agg cac ccc aaa aag ctg acc cct tta gcc tac aag cag ttt atc			144
Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile			

35	40	45	
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Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly			
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aag atc tcc aga aac tcc gag cga ttt aag gaa ctc acc ccc aat tac	240		
Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr			
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Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg			
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ctg atg act cag agg tgt aag gac aag ttg aac gct ttg gcc atc tcg	336		
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser			
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gtg atg aac cag tgg cca gga gtg aaa ctg cgg gtg acc gag ggc tgg	384		
Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp			
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gac gaa gat ggc cac cac tca gag gag tct ctg cac tac gag ggc cgc	432		
Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg			
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Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val			
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Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu			
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Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu			
260 265 270			

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Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu	
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Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr	
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Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu	
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Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr	
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gct cca ggt gct gcc gac gct ccg ggt gcg ggg gcc acc gcg ggc atc	1296
Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile	
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His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp	
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Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser	
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Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu Leu Leu	
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Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg Val Val	
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Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala Tyr Lys	
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Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser Gly Arg	
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Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu Leu Thr	
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Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly	
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gcc gac cgc ctc atg acc cag cgc tgc aag gac cgc ctg aac tcg ctg	392
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu	
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Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr	
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Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr	
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Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys	
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Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val	
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Asp Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe Ser Asp	
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Val Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln	
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Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala	
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His Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala Arg Phe	
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Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val	
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Ala Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr	
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cac gtg gcc ctc ggg gcc tac gcc ccg ctc aca aag cat ggg aca ctg	1064
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Leu Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser Phe His	
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Pro Leu Gly Met Ser Gly Ala Gly Ser	
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Val Pro Gly Val Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
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Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
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Val Leu Ala Ala Asp Ala Ser Gly Arg Val Val Pro Thr Pro Val Leu	
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Glu Thr Glu Trp Pro Pro Arg Lys Leu Leu Leu Thr Pro Trp His Leu	
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Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu	
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gcc gtg ggc gtg ttc gcg ccg ctc acc gcg cac ggg acg ctg ctg gtg	1008
Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val	
325 330 335	
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Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn	
85 90 95	

gct gac agg ctg atg acc aag cgc tgt aag gac aag tta aat tcg ttg	336
Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu	
100 105 110	

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Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr	
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gaa ggc tgg gat gag gat ggt cac cat tta gaa gaa tct ttg cac tat	432
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Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys	
145 150 155 160	

tat ggg atg cta tcc agg ctt gca gtg gag gca gga ttc gac tgg gtc	528
Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val	
165 170 175	
tat tat gaa tct aaa gcc cac ata cac tgc tct gtc aaa gca gaa aat	576
Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn	
180 185 190	
tca gtg gct gct aaa tca gga gga tgt ttt cct ggg tct ggg acg gtg	624
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val	
195 200 205	
aca ctt ggt gat ggg acg agg aaa ccc atc aaa gat ctt aaa gtg ggc	672
Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly	
210 215 220	
gac cgg gtt ttg gct gca gac gag aag gga aat gtc tta ata agc gac	720
Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp	
225 230 235 240	
ttt att atg ttt ata gac cac gat ccg aca acg aga agg caa ttc atc	768
Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile	
245 250 255	
gtc atc gag acg tca gaa cct ttc acc aag ctc acc ctc act gcc gcg	816
Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala	
260 265 270	
cac cta gtt ttc gtt gga aac tct tca gca gct tcg ggt ata aca gca	864
His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala	
275 280 285	
aca ttt gcc agc aac gtg aag cct gga gat aca gtt tta gtg tgg gaa	912
Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu	
290 295 300	
gac aca tgc gag agc ctc aag agc gtt aca gtg aaa agg att tac act	960
Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr	
305 310 315 320	
gag gag cac gag ggc tct ttt gcg cca gtc acc gcg cac gga acc ata	1008
Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile	
325 330 335	
ata gtg gat cag gtg ttg gca tcg tgc tac gcg gtc att gag aac cac	1056
Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His	
340 345 350	
aaa tgg gca cat tgg gct ttt gcg ccg gtc agg ttg tgt cac aag ctg	1104
Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu	
355 360 365	
atg acg tgg ctt ttt ccg gct cgt gaa tca aac gtc aat ttt cag gag	1152
Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu	
370 375 380	

gat ggt atc cac tgg tac tca aat atg ctg ttt cac atc ggc tct tgg 1200
Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
385 390 395 400

tga	1251
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<400> 10
Met Val Glu Met Leu Leu Leu Thr Arg Ile Leu Leu Val Gly Phe Ile
  1             5             10             15
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Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
35 40 45

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr
65 70 75 80

Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu
 . 100 105 110

Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys
145 150 155 160

Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
180 185 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val
195 200 205

His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly
210 215 220

Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp
225 230 235 240

Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr
245 250 255

Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Leu Thr Ala Ala
260 265 270

His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly
275 280 285

Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln
290 295 300

Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser
305 310 315 320

Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro
325 330 335

Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys
340 345 350

Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Trp Ala Phe Ala Pro
355 360 365

Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala
370 375 380

Ile Pro Thr Ala Ala Thr Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
385 390 395 400

Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
405 410 415

Pro Leu Gly Met Val Ala Pro Ala Ser
420 425

<210> 11

<211> 396

<212> PRT

<213> murine Dhh

<400> 11

Met Ala Leu Pro Ala Ser Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
1 5 10 15

Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
20 25 30

Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
35 40 45

Val Pro Ser Met Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
50 55 60

Gly	Arg	Val	Thr	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn		
65					70					75					80		
Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Ser	Gly	Ala	Asp		
				85					90					95			
Arg	Leu	Met	Thr	Glu	Arg	Cys	Lys	Glu	Arg	Val	Asn	Ala	Leu	Ala	Ile		
			100					105					110				
Ala	Val	Met	Asn	Met	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly		
		115					120					125					
Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly		
	130					135					140						
Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly		
145					150					155					160		
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr		
				165					170					175			
Glu	Ser	Arg	Asn	His	Ile	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu		
			180					185					190				
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu		
		195					200					205					
Arg	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp		
	210					215					220						
Val	Leu	Ala	Ala	Asp	Ala	Ala	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu		
225					230					235					240		
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val		
				245					250					255			
Glu	Thr	Glu	Arg	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu		
				260				265					270				
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro		
		275					280					285					
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly		
	290					295					300						
Gly	Asp	Ala	Leu	Gln	Pro	Ala	Arg	Val	Ala	Arg	Val	Ala	Arg	Glu	Glu		
305					310					315				320			
Ala	Val	Gly	Val	Phe	Ala	Pro	Leu	Thr	Ala	His	Gly	Thr	Leu	Leu	Val		
				325					330					335			
Asn	Asp	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Leu	Glu	Ser	His	Gln	Trp		
			340					345					350				
Ala	His	Arg	Ala	Phe	Ala	Pro	Leu	Arg	Leu	Leu	His	Ala	Leu	Gly	Ala		
		355					360						365				

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly
385 390 395

<210> 12

<211> 411

<212> PRT

<213> murine Ihh

<400> 12

Met Ser Pro Ala Trp Leu Arg Pro Arg Leu Arg Phe Cys Leu Phe Leu
1 5 10 15

Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
20 25 30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
35 40 45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
50 55 60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
65 70 75 80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
85 90 95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
100 105 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
115 120 125

Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
130 135 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145 150 155 160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
165 170 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
180 185 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
195 200 205

Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
210 215 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
225 230 235 240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala
 245 250 255
 Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
 260 265 270
 Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala
 275 280 285
 His Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
 290 295 300
 Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
 305 310 315 320
 Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly
 325 330 335
 Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
 340 345 350
 Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe Pro
 355 360 365
 Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
 370 375 380
 Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
 385 390 395 400
 Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
 405 410

<210> 13
 <211> 437
 <212> PRT
 <213> murine Shh

<400> 13
 Met Leu Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser
 1 5 10 15
 Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly
 20 25 30
 Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
 35 40 45
 Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
 50 55 60
 Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
 65 70 75 80
 Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp
 85 90 95

Arg	Leu	Met	Thr	Gln	Arg	Cys	Lys	Asp	Lys	Leu	Asn	Ala	Leu	Ala	Ile	100	105	110
Ser	Val	Met	Asn	Gln	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly	115	120	125
Trp	Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	130	135	140
Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Ser	Lys	Tyr	Gly	145	150	155
Met	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	165	170	175
Glu	Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	180	185	190
Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Ala	Thr	Val	His	Leu	195	200	205
Glu	Gln	Gly	Gly	Thr	Lys	Leu	Val	Lys	Asp	Leu	Arg	Pro	Gly	Asp	Arg	210	215	220
Val	Leu	Ala	Ala	Asp	Asp	Gln	Gly	Arg	Leu	Leu	Tyr	Ser	Asp	Phe	Leu	225	230	235
Thr	Phe	Leu	Asp	Arg	Asp	Glu	Gly	Ala	Lys	Lys	Val	Phe	Tyr	Val	Ile	245	250	255
Glu	Thr	Leu	Glu	Pro	Arg	Glu	Arg	Leu	Leu	Leu	Thr	Ala	Ala	His	Leu	260	265	270
Leu	Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Gly	Pro	Thr	Pro	Gly	Pro	Ser	275	280	285
Ala	Leu	Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val	290	295	300
Ala	Glu	Arg	Gly	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser	305	310	315
Val	Thr	Leu	Arg	Glu	Glu	Glu	Ala	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Ala	325	330	335
His	Gly	Thr	Ile	Leu	Ile	Asn	Arg	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	340	345	350
Ile	Glu	Glu	His	Ser	Trp	Ala	His	Arg	Ala	Phe	Ala	Pro	Phe	Arg	Leu	355	360	365
Ala	His	Ala	Leu	Leu	Ala	Ala	Leu	Ala	Pro	Ala	Arg	Thr	Asp	Gly	Gly	370	375	380
Gly	Gly	Gly	Ser	Ile	Pro	Ala	Ala	Gln	Ser	Ala	Thr	Glu	Ala	Arg	Gly	385	390	395
																		400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His
405 410 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
420 425 430

Ala Val Lys Ser Ser
435

<210> 14

<211> 418

<212> PRT

<213> zebrafish Shh

<400> 14

Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
1 5 10 15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
50 55 60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
100 105 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
115 120 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
145 150 155 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
195 200 205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
210 215 220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
 225 230 235 240
 Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
 245 250 255
 Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
 260 265 270
 Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
 275 280 285
 Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
 290 295 300
 Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
 305 310 315 320
 Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
 325 330 335
 Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
 340 345 350
 Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
 355 360 365
 Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn
 370 375 380
 Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr
 385 390 395 400
 Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
 405 410 415

Ser Ser

<210> 15

<211> 475

<212> PRT

<213> Homo sapien Shh

<220>

<223> Xaa at position 463 is any or unknown amino acid

<400> 15

Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
 1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
 20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
 35 40 45

Pro	Asn	Val	Ala	Glu	Lys	Thr	Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly	50	55	60	
Lys	Ile	Ser	Arg	Asn	Ser	Glu	Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr	65	70	75	80
Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	85	90	95	
Leu	Met	Thr	Gln	Arg	Cys	Lys	Asp	Lys	Leu	Asn	Ala	Leu	Ala	Ile	Ser	100	105	110	
Val	Met	Asn	Gln	Trp	Pro	Gly	Val	Lys	Leu	Arg	Val	Thr	Glu	Gly	Trp	115	120	125	
Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	130	135	140	
Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Ser	Lys	Tyr	Gly	Met	145	150	155	160
Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu	165	170	175	
Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala	180	185	190	
Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Ala	Thr	Val	His	Leu	Glu	195	200	205	
Gln	Gly	Gly	Thr	Lys	Leu	Val	Lys	Asp	Leu	Ser	Pro	Gly	Asp	Arg	Val	210	215	220	
Leu	Ala	Ala	Asp	Asp	Gln	Gly	Arg	Leu	Leu	Tyr	Ser	Asp	Phe	Leu	Thr	225	230	235	240
Phe	Leu	Asp	Arg	Asp	Asp	Gly	Ala	Lys	Lys	Val	Phe	Tyr	Val	Ile	Glu	245	250	255	
Thr	Arg	Glu	Pro	Arg	Glu	Arg	Leu	Leu	Leu	Thr	Ala	Ala	His	Leu	Leu	260	265	270	
Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Ala	Thr	Gly	Glu	Pro	Glu	Ala	Ser	275	280	285	
Ser	Gly	Ser	Gly	Pro	Pro	Ser	Gly	Gly	Ala	Leu	Gly	Pro	Arg	Ala	Leu	290	295	300	
Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val	Ala	Glu	305	310	315	320
Arg	Asp	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser	Val	Thr	325	330	335	
Leu	Ser	Glu	Glu	Ala	Ala	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Ala	Gln	Gly	340	345	350	

Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu
 355 360 365
 Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
 370 375 380
 Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
 385 390 395 400
 Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
 405 410 415
 Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
 420 425 430
 His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
 435 440 445
 Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser
 450 455 460
 Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
 465 470 475

<210> 16

<211> 411

<212> PRT

<213> Homo sapien Ihh

<400> 16

Met Ser Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu
 1 5 10 15
 Leu Leu Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg
 20 25 30
 Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
 35 40 45
 Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
 50 55 60
 Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65 70 75 80
 Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
 85 90 95
 Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
 100 105 110
 Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
 115 120 125
 Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
 130 135 140



His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145 150 155 160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
165 170 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
180 185 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
195 200 205

Gln Val Arg Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg
210 215 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe
225 230 235 240

Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro His Arg Leu Arg Ala
245 250 255

Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
260 265 270

Pro Ala His Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala
275 280 285

Arg Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
290 295 300

Leu Val Ala Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
305 310 315 320

Ser Thr His Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly
325 330 335

Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
340 345 350

Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His
355 360 365

Ser Leu Ala Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr
370 375 380

Pro Gln Leu Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser
385 390 395 400

Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
405 410

<210> 17

<211> 396

<212> PRT

<213> Homo sapien Dhh

<400> 17

Met	Ala	Leu	Leu	Thr	Asn	Leu	Leu	Pro	Leu	Cys	Cys	Leu	Ala	Leu	Leu	1	5	10	15
Ala	Leu	Pro	Ala	Gln	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Pro	Val	Gly	Arg	20	25	30	
Arg	Arg	Tyr	Ala	Arg	Lys	Gln	Leu	Val	Pro	Leu	Leu	Tyr	Lys	Gln	Phe	35	40	45	
Val	Pro	Gly	Val	Pro	Glu	Arg	Thr	Leu	Gly	Ala	Ser	Gly	Pro	Ala	Glu	50	55	60	
Gly	Arg	Val	Ala	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn	65	70	75	80
Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Ser	Gly	Ala	Asp	85	90	95	
Arg	Leu	Met	Thr	Glu	Arg	Cys	Lys	Glu	Arg	Val	Asn	Ala	Leu	Ala	Ile	100	105	110	
Ala	Val	Met	Asn	Met	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly	115	120	125	
Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly	130	135	140	
Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly	145	150	155	160
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	165	170	175	
Glu	Ser	Arg	Asn	His	Val	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu	180	185	190	
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu	195	200	205	
Trp	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp	210	215	220	
Val	Leu	Ala	Ala	Asp	Ala	Ser	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu	225	230	235	240
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val	245	250	255	
Glu	Thr	Glu	Trp	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu	260	265	270	
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro	275	280	285	
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly	290	295	300	

Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305 310 315 320

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
325 330 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
340 345 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
385 390 395

<210> 18

<211> 416

<212> PRT

<213> Zebrafish Thh

<400> 18

Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
1 5 10 15

Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
20 25 30

Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
85 90 95

Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
100 105 110

Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
145 150 155 160

Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
 180 185 190
 Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val
 195 200 205
 Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly
 210 215 220
 Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp
 225 230 235 240
 Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile
 245 250 255
 Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala
 260 265 270
 His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala
 275 280 285
 Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu
 290 295 300
 Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr
 305 310 315 320
 Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile
 325 330 335
 Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His
 340 345 350
 Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu
 355 360 365
 Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
 370 375 380
 Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
 385 390 395 400
 Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
 405 410 415

<210> 19
 <211> 1416
 <212> DNA
 <213> Drosophila HH

<220>
 <221> CDS
 <222> (1)..(1413)

<400> 19
 atg gat aac cac agc tca gtg cct tgg gcc agt gcc gcc agt gtc acc 48

Met	Asp	Asn	His	Ser	Ser	Val	Pro	Trp	Ala	Ser	Ala	Ala	Ser	Val	Thr	
1				5					10					15		
tgt	ctc	tcc	ctg	gga	tgc	caa	atg	cca	cag	ttc	cag	ttc	cag	ttc	cag	96
Cys	Leu	Ser	Leu	Gly	Cys	Gln	Met	Pro	Gln	Phe	Gln	Phe	Gln	Phe	Gln	
			20					25					30			
ctc	caa	atc	cgc	agc	gag	ctc	cat	ctc	cgc	aag	ccc	gca	aga	aga	acg	144
Leu	Gln	Ile	Arg	Ser	Glu	Leu	His	Leu	Arg	Lys	Pro	Ala	Arg	Arg	Thr	
		35					40					45				
caa	acg	atg	cgc	cac	att	gcg	cat	acg	cag	cgt	tgc	ctc	agc	agg	ctg	192
Gln	Thr	Met	Arg	His	Ile	Ala	His	Thr	Gln	Arg	Cys	Leu	Ser	Arg	Leu	
	50					55					60					
acc	tct	ctg	gtg	gcc	ctg	ctg	ctg	atc	gtc	ttg	ccg	atg	gtc	ttt	agc	240
Thr	Ser	Leu	Val	Ala	Leu	Leu	Leu	Ile	Val	Leu	Pro	Met	Val	Phe	Ser	
	65				70				75					80		
ccg	gct	cac	agc	tgc	ggc	cct	ggc	cga	gga	ttg	ggc	cgt	cat	agg	gcg	288
Pro	Ala	His	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Leu	Gly	Arg	His	Arg	Ala	
				85				90						95		
cgc	aac	ctg	tat	ccg	ctg	gtc	ctc	aag	cag	aca	att	ccc	aat	cta	tcc	336
Arg	Asn	Leu	Tyr	Pro	Leu	Val	Leu	Lys	Gln	Thr	Ile	Pro	Asn	Leu	Ser	
			100					105					110			
gag	tac	acg	aac	agc	gcc	tcc	gga	cct	ctg	gag	ggc	gtg	atc	cgt	cgg	384
Glu	Tyr	Thr	Asn	Ser	Ala	Ser	Gly	Pro	Leu	Glu	Gly	Val	Ile	Arg	Arg	
		115					120					125				
gat	tcg	ccc	aaa	ttc	aag	gac	ctc	gtg	ccc	aac	tac	aac	agg	gac	atc	432
Asp	Ser	Pro	Lys	Phe	Lys	Asp	Leu	Val	Pro	Asn	Tyr	Asn	Arg	Asp	Ile	
	130					135					140					
ctt	ttc	cgt	gac	gag	gaa	ggc	acc	gga	gcg	gat	ggc	ttg	atg	agc	aag	480
Leu	Phe	Arg	Asp	Glu	Glu	Gly	Thr	Gly	Ala	Asp	Gly	Leu	Met	Ser	Lys	
	145				150				155						160	
cgc	tgc	aag	gag	aag	cta	aac	gtg	ctg	gcc	tac	tcg	gtg	atg	aac	gaa	528
Arg	Cys	Lys	Glu	Lys	Leu	Asn	Val	Leu	Ala	Tyr	Ser	Val	Met	Asn	Glu	
				165					170					175		
tgg	ccc	ggc	atc	cgg	ctg	ctg	gtc	acc	gag	agc	tgg	gac	gag	gac	tac	576
Trp	Pro	Gly	Ile	Arg	Leu	Leu	Val	Thr	Glu	Ser	Trp	Asp	Glu	Asp	Tyr	
			180					185					190			
cat	cac	ggc	cag	gag	tcg	ctc	cac	tac	gag	ggc	cga	gcg	gtg	acc	att	624
His	His	Gly	Gln	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Thr	Ile	
		195				200						205				
gcc	acc	tcc	gat	cgc	gac	cag	tcc	aaa	tac	ggc	atg	ctc	gct	cgc	ctg	672
Ala	Thr	Ser	Asp	Arg	Asp	Gln	Ser	Lys	Tyr	Gly	Met	Leu	Ala	Arg	Leu	
	210					215					220					
gcc	gtc	gag	gct	gga	ttc	gat	tgg	gtc	tcc	tac	gtc	agc	agg	cgc	cac	720
Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Ser	Tyr	Val	Ser	Arg	Arg	His	

225	230	235	240	
atc tac tgc tcc gtc aag tca gat tgc tgc atc agt tcc cac gtg cac				768
Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His				
	245	250	255	
ggc tgc ttc acg ccg gag agc aca gcg ctg ctg gag agt gga gtc cgg				816
Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg				
	260	265	270	
aag ccg ctc ggc gag ctc tct atc gga gat cgt gtt ttg agc atg acc				864
Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr				
	275	280	285	
gcc aac gga cag gcc gtc tac agc gaa gtg atc ctc ttc atg gac cgc				912
Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg				
	290	295	300	
aac ctc gag cag atg caa aac ttt gtg cag ctg cac acg gac ggt gga				960
Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly				
	305	310	315	320
gca gtg ctc acg gtg acg ccg gct cac ctg gtt agc gtt tgg cag ccg				1008
Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro				
	325	330	335	
gag agc cag aag ctc acg ttt gtg ttt gcg cat cgc atc gag gag aag				1056
Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys				
	340	345	350	
aac cag gtg ctc gta cgg gat gtg gag acg ggc gag ctg agg ccc cag				1104
Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln				
	355	360	365	
cga gtg gtc aag ttg ggc agt gtg cgc agt aag ggc gtg gtc gcg ccg				1152
Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro				
	370	375	380	
ctg acc cgc gag ggc acc att gtg gtc aac tgc gtg gcc gcc agt tgc				1200
Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys				
	385	390	395	400
tat gcg gtg atc aac agt cag tgc ctg gcc cac tgg gga ctg gct ccc				1248
Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro				
	405	410	415	
atg cgc ctg ctg tcc acg ctg gag gcg tgg ctg ccc gcc aag gag cag				1296
Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln				
	420	425	430	
ttg cac agt tgc ccg aag gtg gtg agc tgc gcg cag cag cag aat ggc				1344
Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly				
	435	440	445	
atc cat tgg tat gcc aat gcg ctc tac aag gtc aag gac tac gtg ctg				1392
Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu				
	450	455	460	

ccg cag agc tgg cgc cac gat tga
 Pro Gln Ser Trp Arg His Asp
 465 470

1416

<210> 20
 <211> 471
 <212> PRT
 <213> Drosophila HH

<400> 20
 Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
 1 5 10 15
 Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln
 20 25 30
 Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr
 35 40 45
 Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu
 50 55 60
 Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser
 65 70 75 80
 Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala
 85 90 95
 Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser
 100 105 110
 Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg
 115 120 125
 Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile
 130 135 140
 Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys
 145 150 155 160
 Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
 165 170 175
 Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
 180 185 190
 His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
 195 200 205
 Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
 210 215 220
 Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
 225 230 235 240

Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
 245 250 255
 Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg
 260 265 270
 Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr
 275 280 285
 Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg
 290 295 300
 Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly
 305 310 315 320
 Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro
 325 330 335
 Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys
 340 345 350
 Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln
 355 360 365
 Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro
 370 375 380
 Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys
 385 390 395 400
 Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro
 405 410 415
 Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln
 420 425 430
 Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly
 435 440 445
 Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu
 450 455 460
 Pro Gln Ser Trp Arg His Asp
 465 470

<210> 21

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: degenerate
 polypeptide sequence

<220>

<222> 7

<223> Gly, Ala, Val, Leu, Ile, Phe, Tyr or Trp

<220>

<222> 9

<223> Arg, His or Lys

<220>

<222> 44

<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>

<222> 85

<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>

<222> 93

<223> Lys, Arg, His, Asn or Gln

<220>

<222> 98

<223> Lys, Arg or His

<220>

<222> 112

<223> Ser, Thr, Tyr, Trp or Phe

<220>

<222> 132

<223> Lys, Arg or His

<220>

<222> 137

<223> Met, Cys, Ser or Thr

<220>

<222> 139

<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>

<222> 181

<223> Leu, Val, Met, Thr or Ser

<220>

<222> 183

<223> His, Phe, Tyr, Ser, Thr, Met or Cys

<220>

<222> 185

<223> Gln, Asn, Glu, or Asp

<220>

<222> 186

<223> His, Phe, Tyr, Thr, Gln, Asn, Glu or Asp

<220>

<222> 189

<223> Gln, Asn, Glu, Asp, Thr, Ser, Met or Cys

<220>
 <222> 191
 <223> Ala, Gly, Cys, Leu, Val or Met

 <220>
 <222> 196
 <223> Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser, Thr or Cys

 <220>
 <222> 200
 <223> Arg, Lys, Met or Ile

 <220>
 <222> 206
 <223> Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr or Met

 <220>
 <222> 207
 <223> Ala, Gly, Cys, Asp, Asn, Glu or Gln

 <220>
 <222> 209
 <223> Arg, Lys, Met, Ile, Asn, Asp, Glu or Gln

 <220>
 <222> 211
 <223> Leu, Val, Met or Ile

 <220>
 <222> 212
 <223> Phe, Tyr, Thr, His or Trp

 <220>
 <222> 216
 <223> Ile, Val, Leu or Met

 <220>
 <222> 217
 <223> Met, Cys, Ile, Leu, Val, Thr or Ser

 <220>
 <222> 219
 <223> Leu, Val, Met, Thr or Ser

 <220>
 <223> each Xaa may also be any amino acid.

 <400> 21
 Cys Gly Pro Gly Arg Gly Xaa Gly Xaa Arg Arg His Pro Lys Lys Leu
 1 5 10 15
 Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr
 20 25 30
 Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu
 35 40 45

Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys
50						55				60					
Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	Leu	Met	Thr	Gln	Arg	Cys	Lys
65				70					75					80	
Asp	Lys	Leu	Asn	Xaa	Leu	Ala	Ile	Ser	Val	Met	Asn	Xaa	Trp	Pro	Gly
			85					90						95	
Val	Xaa	Leu	Arg	Val	Thr	Glu	Gly	Trp	Asp	Glu	Asp	Gly	His	His	Xaa
		100					105						110		
Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser
		115					120					125			
Asp	Arg	Asp	Xaa	Ser	Lys	Tyr	Gly	Xaa	Leu	Xaa	Arg	Leu	Ala	Val	Glu
	130					135					140				
Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu	Ser	Lys	Ala	His	Ile	His	Cys
145				150						155					160
Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe
			165					170						175	
Pro	Gly	Ser	Ala	Xaa	Val	Xaa	Leu	Xaa	Xaa	Gly	Gly	Xaa	Lys	Xaa	Val
		180					185						190		
Lys	Asp	Leu	Xaa	Pro	Gly	Asp	Xaa	Val	Leu	Ala	Ala	Asp	Xaa	Xaa	Gly
	195					200						205			
Xaa	Leu	Xaa	Xaa	Ser	Asp	Phe	Xaa	Xaa	Phe	Xaa	Asp	Arg			
	210					215					220				

<210> 22

<211> 167

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: degenerate polypeptide sequence

<220>

<222> 7

<223> Gly, Ala, Val, Leu, Ile, Pro, Phe or Tyr

<220>

<222> 8

<223> Gly, Ala, Val, Leu or Ile

<220>

<222> 9

<223> Gly, Ala, Val, Leu, Ile, Lys, His or Arg

<220>

<222> 12
<223> Lys, Arg or His

<220>
<222> 13
<223> Phe, Trp, Tyr or an amino acid gap

<220>
<222> 14
<223> Gly, Ala, Val, Leu, Ile or an amino acid gap

<220>
<222> 17
<223> Asn, Gln, His, Arg or Lys

<220>
<222> 19
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<222> 22
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<222> 27
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<222> 29
<223> Ser, Thr, Gln or Asn

<220>
<222> 30
<223> Met, Cys, Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<222> 31
<223> Gly, Ala, Val, Leu, Ile or Pro

<220>
<222> 33
<223> Arg, His or Lys

<220>
<222> 40
<223> Gly, Ala, Val, Leu, Ile, Pro, Arg, His or Lys

<220>
<222> 41
<223> Gly, Ala, Val, Leu, Ile, Phe or Tyr

<220>
<222> 44
<223> Arg, His or Lys

<220>
<222> 45

<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<222> 46
<223> Thr or Ser

<220>
<222> 48
<223> Gly, Ala, Val, Leu, Ile, Asn or Gln

<220>
<222> 53
<223> Arg, His or Lys

<220>
<222> 54
<223> Asp or Glu

<220>
<222> 71
<223> Ser or Thr

<220>
<222> 79
<223> Glu, Asp, Gln or Asn

<220>
<222> 83
<223> Glu or Asp

<220>
<222> 84
<223> Arg, His or Lys

<220>
<222> 85
<223> Gly, Ala, Val, Leu or Ile

<220>
<222> 87
<223> Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
<222> 95
<223> Met, Cys, Gln, Asn, Arg, Lys or His

<220>
<222> 100
<223> Arg, His or Lys

<220>
<222> 107
<223> Trp, Phe, Tyr, Arg, His or Lys

<220>
<222> 114
<223> Gly, Ala, Val, Leu, Ile, Ser, Thr, Tyr or Phe

<220>
<222> 115
<223> Gln, Asn, Asp or Glu

<220>
<222> 116
<223> Asp or Glu

<220>
<222> 125
<223> Gly, Ala, Val, Leu, or Ile

<220>
<222> 134
<223> Arg, His or Lys

<220>
<222> 135
<223> Asn, Gln, Thr or Ser

<220>
<222> 139
<223> Gly, Ala, Val, Leu, Ile, Ser, Thr, Met or Cys

<220>
<222> 141
<223> Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
<222> 157
<223> Arg, His or Lys

<220>
<222> 158
<223> Asn, Gln, Gly, Ala, Val, Leu or Ile

<220>
<222> 160
<223> Gly, Ala, Val, Leu or Ile

<220>
<222> 162
<223> Gly, Ala, Val, Leu, Ile, Ser, Thr or Cys

<220>
<222> 166
<223> Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
<222> 167
<223> Asp or Glu

<400> 22
Cys Gly Pro Gly Arg Gly Xaa Xaa Xaa Arg Arg Xaa Xaa Xaa Pro Lys
1 5 10 15

Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
 20 25 30
 Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
 35 40 45
 Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
 50 55 60
 Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg
 65 70 75 80
 Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp
 85 90 95
 Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His
 100 105 110
 His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr
 115 120 125
 Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala
 130 135 140
 Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa
 145 150 155 160
 His Xaa Ser Val Lys Xaa Xaa
 165

<210> 23

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: primer

<400> 23

gcgcgcttcg aagcgaggca gccagcgagg gagagagcga gcgggcgagc cggagcgagg 60

aaatcgatgc gcgc

74

<210> 24

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: primer

<400> 24

gcgcgcagat ctgggaaagc gcaagagaga gcgcacacgc acacacccgc cgcgcgact 60

cgggatccgc gcgc

74

<210> 25
<211> 996
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: gene
activation construct

<400> 25
cgaagcgagg cagccagcga gggagagagc gagcgggcca gccggagcga ggaaatcgaa 60
ggttcgaatc cttccccac caccatcact ttcaaaagtc cgaaagaatc tgctccctgc 120
ttgtgtgttg gaggtcgctg agtagtgccg gagtaaaatt taagctacaa caaggcaagg 180
cttgaccgac aattgcatga agaatctgct tagggttagg cgttttgccc tgcttcgcca 240
tgtacggggc agatatacgc gttgacattg attattgact agttattaat agtaatcaat 300
tacgggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa 360
tggcccgctt ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt 420
tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggact atttacggta 480
aactgcccac ttggcagtac atcaagtgtg tcatatgccg agtacgcccc ctattgacgt 540
caatgacggg aaatggcccg cctggcatta tgcccagtac atgaccttat gggactttcc 600
tacttggcag tacatctacg tattagtcac cgctattacc atggtgatgc ggttttggca 660
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<220>
<223> Description of Artificial Sequence: antisense
construct

<400> 26

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26

<210> 27

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: antisense
construct

<400> 27

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26

<210> 28

<211> 26

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: antisense
construct

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26